Translation

PATENT COOPERATION TREATY

PCT/JP2003/002602

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P023P01	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/JP2003/002602	International filing date (*day/month/year*) 05 March 2003 (05.03.2003)	Priority date (*day/month/year*) 29 March 2002 (29.03.2002)
International Patent Classification (IPC) or national classification and IPC A61K 48/00, 45/00, 9/51, 9/08, 38/18, 38/21, A61P 1/16, 35/00		
Applicant JAPAN SCIENCE AND TECHNOLOGY CORPORATION		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
31 July 2003 (31.07.2003)	27 February 2004 (27.02.2004)
Name and mailing address of the IPEA/JP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/JP2003/002602

I. Basis of the report

1. With regard to the **elements** of the international application:*

☒ the international application as originally filed

☐ the description:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the claims:

pages _____, as originally filed
pages _____, as amended (together with any statement under Article 19
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the drawings:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the sequence listing part of the description:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this A[illegible] in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23[illegible])

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☒ contained in the international application in written form.

☒ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 8

because:

☒ the said international application, or the said claims Nos. 8
relate to the following subject matter which does not require an international preliminary examination *(specify)*:

The subject matter of claim 8 relates to a method for treatment of the human body by therapy, which does not require an international preliminary examination by the International Preliminary Examining Authority in accordance with PCT Articles 34(4)(a)(i) and Rule 67.1(iv).

☐ the description, claims or drawings *(indicate particulars below)* or said claims Nos. _____
are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. _____ are so inadequately supported
by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 8 .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-7	YES
	Claims		NO
Inventive step (IS)	Claims	6	YES
	Claims	1-5, 7	NO
Industrial applicability (IA)	Claims	1-7	YES
	Claims		NO

2. Citations and explanations

Document 1: WO, 01-64930, A1 (Japan Science and Technology Corp.), 7 September, 2001 (07.09.01), & EP, 1262555, A1, & JP, 2001-316298, A

(1) Document 1 describes hollow nanoparticles made of hepatitis B virus surface antigen protein (HBsAg) and also describes that a gene encoding protein or the like for treating cancers, which is so incorporated that the expression thereof is possible, is encapsulated, as a substance to be transferred into cells, in the hollow nanoparticles (line 4, page 8 to line 3, page 9; Examples G and H). Further, it describes that such hollow nanoparticles are highly efficient carriers to convey a substance specifically to liver cells (lines 19-24, page 6).

Document 1 also describes the preparation of modified particles which are capable of presenting an optional substance to be transferred into cells on the surfaces of the particles while maintaining the particle-forming capability of h[illegible]particles (Examples C, 4 and 5), as well as the expression of an HBsAg gene fused with a gene enco[illegible] molecule to a specific cell surface molecule such as EGF and its presentation on the nanoparticle surfac[illegible]amples D-F and 6-9). Also, in view of the fact that generally in the field related to drug delivery systems, the use of an effective medical substance such as a bioactive protein directly bonded to a carrier is a commonly known matter before the priority date of the present application without needing to cite literature, a person skilled in the art could have easily conceived, based on the above description of document 1 and the commonly known matter stated above, that, for the purpose of application, a substance to be transferred into cells for treating diseases is directly bonded to HBsAa, a carrier, and that in this process, instead of the abovementioned bond particle, a gene of a commonly-known protein for treating diseases such as Interferon or HGF is fused with an HBsAg gene as a gene encoding a substance to be transferred into cells and introduced so as to obtain hollow nanoparticles comprising the fused genes subjected to expression.

Note that in claims 1-5 and 7, specified matters of the invention are not limited to the mode of adopting, as "substances to be transferred into cells," a bioactive protein that is expressed in the form in which it actually fuses with an HBsAg protein and is active, and is clearly known to be actually capable of producing an advantageous therapeutic effect.

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

(1) The Examples shown in the specification simply confirm that a gene encoding a fused protein of hollow nanoparticle protein + protein as a substance to be transferred into cells is expressed in target cells by means of SDS-PAGE or western blotting. It is not supported by sufficiently concrete data results or technical grounds to replace such data results in the specifications or the drawings on all the drugs included in claims 1-7 that a desired bioactive function is actually fulfilled and that the function attains effectiveness in treating diseases even when as "a substance to be transferred into cells," an optional one is adopted together with hollow nanoparticles (particularly when an optional bioactive protein other than interferon, HGF and GFP adopted in the specification of the present application is adopted).

(2) As "hollow nanoparticles made of a protein which is capable of recognizing specific cells and forming particles" defined in claim 1, only HBsAg particles are supported in and disclosed in the specification in the sense of PCT Article 6 and Article 5 respectively. Further, as to "hollow nanoparticles made of a protein which is capable of recognizing specific cells and forming particles," the scope of substances having such properties is unable to be defined even taking into account common general technical knowledge at the time when the application was filed, and claim 1 also does not satisfy the requirement for clarity in PCT Article 6.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of : V

(2) Document 1 cited in the ISR does not describe that Interferon (IFN) or a liver cell growth factor (HGF) is expressed in the form in which it is fused with hollow nanoparticles made of HBsAg protein and is active, and is actually capable of producing an advantageous therapeutic effect, and this does not appear to be obvious to a person skilled in the art from the description of document 1.